

Medical School Loan Repayment Program

Grant Award Details

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Grant Type: New Faculty Physician Scientist

Grant Number: RN3-06455-1.2

Investigator:

Name: Ali Nsair

Type: PI

Award Value: \$120,312

Status: Closed

Grant Application Details

Application Title: Human Induced Pluripotent Stem Cell-Derived Cardiovascular Progenitor Cells for Cardiac Cell Therapy.

Public Abstract: Despite therapeutic advances, cardiovascular disease remains a leading cause of mortality and morbidity in California. Regenerative therapies that restore normal function after a heart attack would have an enormous societal and financial impact. Although very promising, regenerative cardiac cell therapy faces a number of challenges and technological hurdles. Human induced pluripotent stem cells (hiPSC) allow the potential to deliver patient specific, well-defined cardiac progenitor cells (CPC) for regenerative clinical therapies. We propose to translate recent advances in our lab into the development of a novel, well-defined hiPSC-derived CPC therapy. All protocols will be based on clinical-grade, FDA-approvable, animal product-free methods to facilitate preclinical testing in a large animal model.

This application will attempt to translate these findings by:

- Developing techniques and protocols utilizing human induced pluripotent stem cell-derived cardiac progenitor cells at yields adequate to conduct preclinical large animal studies.
- Validation of therapeutic activity will be in small and large animal models of ischemic heart disease by demonstrating effectiveness of hiPSC-derived CPCs in regenerating damaged myocardium post myocardial infarction in small and large animal models.

This developmental candidate and techniques described here, if shown to be a feasible alternative to current approaches, would offer a novel approach to the treatment of ischemic heart disease.

Statement of Benefit to California: Cardiovascular disease remains the leading cause of morbidity and mortality in California and the US costing the healthcare system greater than 300 billion dollars a year. Although current therapies slow progression of heart disease, there are few options to reverse or repair the damaged heart. The limited ability of the heart to regenerate following a heart attack results in loss of function and heart failure. Human clinical trials testing the efficacy of adult stem cell therapy to restore mechanical function after a heart attack, although promising, have had variable results with modest improvements.

The discovery of human induced pluripotent stem cells offers a potentially unlimited renewable source for patient specific cardiac progenitor cells. However, practical application of pluripotent stem cells or their derivatives face a number of challenges and technological hurdles. We have demonstrated that cardiac progenitor cells, which are capable of differentiating into all cardiovascular cell types, are present during normal fetal development and can be isolated from human induced pluripotent stem cells. We propose to translate these findings into a large animal pre-clinical model and eventually to human clinical trials. This could lead to new therapies that would restore heart function after a heart attack preventing heart failure and death. This will have tremendous societal and financial benefits to patients in California and the US in treating heart failure.

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